Food Reviews International

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/lfri20

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To cite this article: Ivan Nastasijevic, Francesco Proscia, Karlo Jurica & Slavica Veskovic-Moracanin (09 Nov 2023): Tracking Antimicrobial Resistance Along the Meat Chain: One Health Context, Food Reviews International, DOI: 10.1080/87559129.2023.2279590

To link to this article: https://doi.org/10.1080/87559129.2023.2279590

FOOD REVIEWS INTERNATIONAL
https://doi.org/10.1080/87559129.2023.2279590

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Tracking Antimicrobial Resistance Along the Meat Chain: One Health Context

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ABSTRACT

Food-borne pathogens and antimicrobial resistance (AMR) represent the significant public health challenges in the 21st century. Increased emergence of AMR in major zoonotic food-borne pathogens (*Salmonella*, *Campylobacter*) and in commensal bacteria (*E. coli*, enterococci), its presence in agro-food (meat) chain and environment, including control/prevention of AMR transfer from food-producing animals to humans via food consumption, is of utmost importance for public health. This review highlights the most relevant risk mitigation strategies for AMR in the meat production chain within One Health context. The monitoring and surveillance systems for AMR in meat chain are presented and briefly discussed, including sampling schemes, susceptibility testing, clinical resistance and epidemiological cut-off values. The most effective approaches to track and manage AMR in farm-abattoir-meat processing-retail continuum have been recommended, including aspects of international harmonization of critically important antimicrobials for human and veterinary use. The successful AMR monitoring and control in the meat chain can be achieved by evidence-based and integrated approach within One Health context. The application of state-of-the-art technologies and methods for detection and tracking of zoonotic food borne pathogens and AMR, such as Whole Genome Sequencing supported with data processing using Artificial Intelligence (machine learning), can contribute to achieving this goal.

KEYWORDS
AMR; meat chain; food borne; risk mitigation; one health

Introduction

A history of modern applications of antimicrobials in human and veterinary medicine begins with discovery of penicillin in 1928 by Alexander Fleming. This initiated further research on purification of penicillin which started during 1939 by Howard Florey and Ernst Chain at the Sir William Dunn School of Pathology at Oxford University, turning penicillin from an initial laboratory discovery into a life-saving drug. First introduction of antimicrobials in humans occurred in 1941 in 43 years-old policeman who became the first recipient of the Oxford Penicillin for the treatment of a life-threating abscess affecting his eyes, face and lungs. Soon afterwards, the use of penicillin in the 1940s was introduced in British troops in the II World War, in spite that wartime conditions made the industrial production of penicillin difficult[1]. Further development after the war enabling development of industrial-scale production of penicillin revolutionized the health care and approach in human medicine regarding treatment of infectious diseases provoked by pathogenic microorganisms of bacterial origin. It also led to the reduction of child mortality and significantly increased the life expectancy on a global scale.[1]

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Parallel to that, the application of antimicrobials in veterinary medicine, in food-producing animals, also had a prominent role in production of food of animal origin, in particular meat. The first application of antimicrobials to treat infection in animals was recorded in 1935 when synthetic sulfonamide `Prontosil` (sulfochrysoidine) manufactured by `Bayer` (Germany) was used against Gram-positive infections.[2] Later, gramicidin was used to treat massive outbreak of mastitis in cows` herds in the UK in 1940, while penicillin supplies were also tested in 1943 to treat mastitis in order to provide supply of safe milk during wartime.[2,3]

The antimicrobial use (AMU) in large-scale farm operations from the mid-1950s and onwards contributed to maintenance of animal health status in densely populated farm environment by reducing the incidence and intensity of infectious diseases. Consequently, it also led to a global increase of AMU compared to previous decades, with 73% being associated with the livestock industry.[4,5] Such overuse of antimicrobials associated with the frequent misuse (e.g. sub-therapeutic dose) triggered concerns related to antibiotic residues and associated development of antimicrobial resistance (AMR) via horizontal transmission of genes, carriers of resistance in agro-food environment. Subsequently, this jeopardized the treatment of infectious diseases in humans by reducing the options for treating the diseases, including those associated with zoonotic food (meat) borne hazards.

AMR is happening on a global level and in all parts of the world, where a broad range of microorganisms, including pathogens (*Salmonella*, *Campylobacter*) and commensals (*E. coli*, enterococci), show such pattern, thus threatening human and animal health and impacting the whole society.[6] The direct consequences related to the infection with resistant microorganisms can be therefore serious and include prolonged illness, increased mortality rates, longer hospitalizations, reduced protection of patients after surgery and other medical procedures, as well as increased overal costs [6]. In this regard, the AMR is called a “ticking time bomb”[7] and because of such development some countries (e.g. UK) consider including AMR in the National Risk Register of Civil Emergencies being a recognized threat such as coastal floods or terrorist attacks.[2]

This paper aimed to provide a) insight to systemic approach to AMR monitoring, surveillance and reporting systems in the meat chain continuum, aimed for public health protection, and b) to highlight importance of inter-sectoral collaboration and international initiatives in tackling AMR within One Health context.

Materials and methods

A literature review was performed by identifying and analysing published scientific articles (research and review papers, technical reports by international organizations) and databases, published in domains of zoonotic food borne pathogens and related antimicrobial resistance, including the public health impact and originated from the scientific databases such as Web of Science, Scopus, PubMed, EBSCO and CAB Abstracts and the international guidelines. The official websites of selected national AMR monitoring and surveillance schemes were also analysed, including the European Antimicrobial Resistance Surveillance Network (EARS-Net) and European Surveillance of Veterinary Antimicrobial Consumption (ESVAC). The relevant keywords and phrases related to the topic have been identified for the search. A search strategy based on defined keywords was based on Boolean operators (AND, OR, NOT) to combine keywords and narrow down results. These included terms like “AMR AND meat chain”, “AMR AND livestock“, AMR AND food borne disease”, “AMR AND veterinary medicine“, AMR AND risk mitigation”, “AMR AND One Health”, “AMR AND monitoring”. The search was done for the years between 2000 and 2023. The relevance of each source of information included reading through the titles and abstracts of the search results to assess its relevance and eligibility for the given topic. The quality and credibility of the selected articles including consideration of factors like the reputation of the journal, the authors’ credentials, and the methodology used in the research. Once a list of relevant articles has been confirmed, a “snowballing” technique was used to help us to discover more comprehensive and relevant literature. It encompassed the review of their reference lists for additional sources that might not have appeared in the initial search. The selection criteria chosen to identify the relevant articles within the scope of this review and the objectives of this paper were as follow: 1) focus on AMU and specific meat chain-associated AMR in a One Health context; 2) focus on the potential for improvement of inter-sectoral cooperation between environment, veterinary and health authorities to prevent/reduce the occurrence of AMR. The data, as well as monitoring and surveillance programmes on AMU and AMR of the major zoonotic foodborne pathogens with public health importance (*Salmonella, Campylobacter*, methicillin-resistant *Staphylococcus aureus*/MRSA) and indicator bacteria (*E. coli*, *Enterococcus* spp.) were reviewed presenting the status in the European Union/European Economic Area (EU/EEA) countries, with a brief reflection on global importance of AMR in the food (meat chain).

Definitions and classifications of antimicrobials by different global organizations

To raise awareness on the importance of effective patients` treatment and prudent use of antimicrobials (in particular antibiotics) to prevent and reduce development of AMR, World Health Organization (WHO) issued a list of Critically Important Antimicrobials (CIA) – WHO CIA List[8] which was originally developed in 2005 by tripartite engagement of two United Nations agencies, namely Food and Agriculture Organization (FAO) and WHO, together with the World Organization for Animal Health (WOAH).[8] The outcome was threefold: (i) confirmation of the clear evidence of adverse human health consequences due to resistant organisms resulted from non-human usage of antimicrobials that led to increased episodes of treatment failures (including deaths) and increased severity and duration of infections (e.g. fluoroquinolone-resistant human *Salmonella* infections), (ii) evidence that increased non-human usage (overuse) and inadequate use (misuse) of antimicrobials increased the occurrence of resistant bacteria in animals and on/in food of animal origin and consequently increased exposure of humans to these resistance bacteria, including via food, and (iii) recognition that consequences of AMR were particularly severe in cases where pathogens showed resistance to antimicrobials is critically important for human health.[8] Two criteria were used for classification of antimicrobials for human use in categories: Criterion 1 – The antimicrobial class is the sole, or one of the limited available therapies, to treat serious bacterial infections in people, and Criterion 2 - The antimicrobial class is used to treat infections in people caused by either: (1) bacteria that may be transmitted to humans from non-human sources, or (2) bacteria that may acquire resistance genes from non-human sources. Based on these criteria, the antimicrobials are categorized as (i) Critically Important, (ii) Highly Important, and (iii) Important.

On the other hand, WOAH recognized the importance of AMR as a global concern for public and animal helath followed by adoption of the List of Antimicrobials of Veterinary Importance stating that antimicrobial agents are essential drugs for human and animal health and welfare and that animal and plant sectors have a shared responsibility to prevent or minimize AMR selection pressure on both, human and non-human pathogens`.[9] The veterinary antimicrobials are divided into three categories, based on two criterions: Criterion 1 – Response rate to the questionnaire regarding Veterinary Critically Important Antimicrobials (VCIA) where the criterion is met when more than 50% respondents identified the importance of the antimicrobial class in their response to the questionnaire, and Criterion 2 – Treatment of serious animal disease and availability of alternative antimicrobials where criterion was met when compounds within the class were identified as essential against specific infections and there was a lack of sufficient therapeutic alternatives; those categories are as follows: (i) Veterinary Critically Important Antimicrobials – VCIA (meet both criteria 1 & 2), (ii) Veterinary Highly Important Antimicrobials – VHIA (meet criteria 1 or 2), and (iii) Veterinary Important Antimicrobials – VIA (meet neither criteria 1 or 2).[9]

However, these two lists of critically important antimicrobials for human and veterinary medicine, adopted by WHO and WOAH, are not mutually harmonized to provide the most relevant

Table 1. Overview of veterinary critically important (Woah)/critically important antimicrobials (WHO).

	Status	
Antimicrobial family	World Organisation for Animal Health (WOAH) *(animal species)*	World Health Organization (WHO)
†Aminoglycosides *(Spectinomycin, Streptomycin, Dihydrostreptomycin, Framycetin, Kanamycin, Neomycin, Paromomycin, Apramycin, Gentamicin, Tobramycin, Amikacin)*	VCIA *(AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI)*	CIA
Cephalosporins 1 G *(Cefacetrile, Cefalexin, Cefalotin, Cefapyrin, Cefazolin, Cefalonium)*	VCIA *(AVI, BOV, CAP, EQU, LEP, OVI, SUI)*	CIA Cephalosporins (3rd, 4th and 5th generation)
Cephalosporins 2 G *(Cefuroxime)*		
*Cephalosporins 3 G *(Cefoperazone, Ceftiofur, Ceftriaxone)*		
*Cephalosporins 4 G *(Cefquinome)*		
*Macrolides *(Tulathromycin, Erythromycin, Josamycin, Kitasamycin, Spiramycin, Tilmicosin, Tylosin, Mirosamycin, Terdecamycin)*	VCIA *(API, AVI, BOV,CAP, EQU, LEP, OVI, PIS, SUI)*	CIA Macrolides and ketolides
†Penicillins *(Benzylpenicillin, Penethamate hydroxide, Penicillin procaine, Mecillinam, Amoxicillin, Ampicillin, Hetacillin, Amoxicillin Clavulanic Acid, Ticarcillin, Tobicillin, Aspoxicillin, Aspoxicillin, Phenoxymethylpenicillin, Phenethicillin, Cloxacillin, Dicloxacillin, Nafcillin, Oxacillin)*	VCIA *(AVI, BOV, CAM, CAP, EQU, LEP, OVI, SUI)*	CIA Penicillins (antipseudomonal) Penicillins (aminopenicillins) Penicillins (aminopenicillins with ß-lactamase inhibitors)
Phenicols *(Florphenicol, Thiamphenicol)*	VCIA *(AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI)*	HIA
*Quinolones 1 G *(Flumequin, Miloxacin, Nalidixic acid, Oxolinic acid)*	VCIA *(AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI)*	CIA
*Quinolones 2 G *(Ciprofloxacin, Danofloxacin, Difloxacin, Enrofloxacin, Marbofloxacin, Norfloxacin, Ofloxacin, Orbifloxacin)*		
Sulfonamides *(Sulfachlorpyridazine, Sulfadiazine, Sulfadimerazin, Sulfadimethoxine, Sulfadimidine, Sulfadoxine, Sulfafurazole, Sulfaguanidine, Sulfamethazine, Sulfadimethoxazole, Sulfamethoxine, Sulfamonomethoxine, Sulfanilamide, Sulfaquinoxaline, Sulfamethoxypyridazine, Trimethoprim+Sulfonamide, Baquiloprim, Trimethoprim)*	VCIA *(AVI, BOV, CAP, EQU, LEP, OVI, PIS, SUI)*	HIA
Tetracyclines *(Chlortetracycline, Doxycycline, Oxytetracycline, Tetracycline)*	VCIA *(API, AVI, BOV, CAM, CAP, EQU, LEP, OVI, PIS, SUI)*	HIA

VCIA (Veterinary Critically Important Antimicrobial Agents); CIA (Critically Important Antimicrobials for Human Medicine); HIA (Highly Important Antimicrobials).
*Highest priority Critically Important Antibiotics; †High priority Critically Important Antibiotics.
AVI: Avian; EQU: Equine; API: Bee; LEP: Rabbit; BOV: Bovine; OVI: Ovine; CAP: Caprine; PIS: Fish; CAM: Camel; SUI: Swine.

recommendation for protocols to be applied by human medicine and veterinary medicine practitioners (Table 1).

AMR and intensive farming systems – a global health concern

Intensive farming systems, in attempt to satisfy the increased global demand for animal protein, are major driver for AMU on a global scale.[5] In such production systems antimicrobials are frequently used not only to treat food-producing animals against infectious diseases but also to prevent disease development (metaphylaxis), including growth promotion. Consequently, such overuse and misuse of antimicrobials can lead to selective pressure on microorganisms resulting in development and spread of AMR.[10] Such circumstances, which also encompass massive increase of global food trade, have led to the emergence and spread of AMR globally.[11]

In the EU, the AMR issue became one of the top three priority public health threats[12] deserving attention of all relevant stakeholders, e.g. competent and regulatory authorities (health, veterinary, food and environmental agencies), scientific community, food industry and consumers. Therefore, the AMR monitoring is designed to encompass the whole food chain, including public health surveillance and is carried out in accordance with `Zoonoses Directive` (99/2003/EC).[13] Further, EU Commission recently adopted revision of the pharmaceutical legislation recommending One Health approach to combat AMR.[14] In line with these initiatives, the European Centre for Disease Control and Prevention (ECDC) issued several targets to be achieved until 2023, such as: (i) 20% reduction of the total antibiotic consumption in humans, (ii) at least 65% of the total consumption of antibiotics in humans should be effective (use of the right antibiotic), and (iii) reduction of infections by three key antibiotic-resistant bacteria (mainly applied in hospitals). However, in spite of numerous studies related to emergence and spread of AMR and its sources and causes it is still uncertain how much it can be linked with a food chain, in particular meat chain.

To improve understanding of a link between AMR and meat chain relevant data on antimicrobial use in livestock sector (food-producing animals) are of importance. The consumption of veterinary medicinal products (VMPs), including antimicrobials at the European level, was addressed within the scope of ESVAC project based on data reporting protocol and data collection from 31 European countries.[15] The ESVAC project was launched by the European Medicine Agency (EMA) in 2009 in accordance with strategic direction of the EU Commission (EC) to develop a harmonized approach to the collection and reporting of data on the use of antimicrobial agents in animals from the EU Member States (MSs), European Economic Area (EEA) countries (Norway, Liechtenstein, Iceland) and Switzerland. Data are predominantly based on sales of veterinary antibiotic agents. For the purposes of this report, the groups of antimicrobial substances were divided as follows: (i) antimicrobial substances for intestinal use, (ii) antimicrobial substances for intrauterine use, (iii) antimicrobial substances for systemic use, (iv) antimicrobial substances for intramammary use, (v) antimicrobial substances used as antiprotozoals. A denominator for the sales data was established to harmonize the information on the total quantities of antibiotic active substance sold in each country by the animal population that could be potentially treated and it is named as Population Correction Unit (PCU).[15] The PCU includes only food-producing animals, including horses and farmed fish, while data for companion animals (dogs, cats) are not available.[15] The antibiotic consumption per country in the EU/EEA MSs is expressed as mg/PCU. The overview of antibiotic sales for use in treatment of food-producing animals in the EU/EEA is shown in Table 2. This report on antimicrobial VMPS` sales is done by the ESVAC sales advisory expert group of EMA, based on data previously approved by ESVAC National Contact Points in EU/EEA countries. The information originates from VMPs` wholesale and retail sector. The presented data cover all pharmaceutical forms, including premixes for medicated feed (the use of antimicrobial growth promoters is prohibited in ESVAC participating countries). However, presented data should not be used for direct comparison between countries due to differences in reporting and inconsistency related to reporting on animal demography, available VMPs, disease incidence and/or outbreaks in livestock.

The antibiotic consumption (mg/PCU) per country/per biomass appeared to be the lowest in four countries: Norway, Iceland, Sweden and Finland (<20 mg/PCU), while only five countries showed HDI upper 0,9 (Norway, Switzerland, Denmark, Netherlands, and Germany). Low-moderate level (≥20 ≤ 50 mg/PCU) of consumption is observed in twelve countries: Lithuania, Latvia, Luxembourg, United Kingdom, Slovenia, Switzerland, Denmark, Austria, Slovakia, Ireland, Estonia, Netherlands. High-moderate level (≥50 ≤ 100 mg/PCU) was recorded in five countries: Czechia, France, Romania, Croatia, Germany, Belgium. Lastly, high level of antibiotic consumption (≥100 mg/PCU) was observed in nine countries: Greece, Malta, Bulgaria, Portugal, Hungary, Spain, Italy, Poland, Cyprus (Table 2).

However, the scarcity of comprehensive and systematic data on food-producing animals and related farm biosecurity scores in the EU/EEA countries doesn`t provide the opportunity to compare

Table 2. Overview of sales of antibiotic VMPs for food-producing animals, PCU in 1,000 tonnes and sales in mg/PCU in 31 EU/EEA countries in decreasing order per mg/PCU in 2021.[15,16]

Country	Sales (tonnes) for food-producing animals	PCU (1,000 tonnes)	mg/PCU	Human Development Index (HDI)
Norway	5.5	2,196.9	2.5	.944
Iceland	.5	144.8	3.6	.895
Sweden	8.6	787.6	1.9	.898
Finland	8.4	492.0	17.0	.879
Lithuania	6.0	296.6	2.3	.834
Latvia	3.9	152.6	25.5	.810
Luxembourg	1.5	54.2	27.1	.881
United Kingdom	199.5	7,053.9	28.3	.892
Slovenia	5.8	183.7	31.8	.874
Switzerland	25.9	809.8	32.0	.917
Denmark	81.9	2,452.1	33.4	.900
Austria	39.1	945.4	41.3	.881
Slovakia	9.6	229.9	41.7	.830
Ireland	93.2	2,196.1	42.4	.899
Estonia	5.3	114.4	46.6	.840
Netherlands	147.2	3,091.9	47.6	.915
Czechia	35.5	709.0	5.0	.861
France	349.3	6,758.1	51.7	.884
Romania	173.7	2,942.8	59.0	.785
Croatia	2.7	33.8	62.7	.812
Germany	59.7	8,071.2	73.2	.911
Belgium	168.6	1,769.5	95.3	.881
Greece	119.7	1,099.9	108.8	.853
Malta	1.6	14.8	11.5	.829
Bulgaria	48.7	391.3	124.5	.777
Portugal	159.4	1,063.3	149.9	.822
Hungary	131.6	845.8	155.6	.818
Spain	1,296.5	8,245.0	157.2	.869
Italy	661.7	3,812.6	173.5	.872
Poland	775.1	4,417.2	175.5	.834
Cyprus	45.1	152.0	296.5	.845
Total: 31 countries	5,219.6	61,825.1	84.4*	

*aggregated sales (tonnes) for food-producing animals, including horses and farmed fish, normalised by the aggregated PCU (1,000 tonnes).

PCU (Population Correction Unit); VMPs: Veterinary Medical Products; EU/EEA: European Union/European Economic Areas.

AMU rates with farm biosecurity scores (e.g. broilers, pigs, dairy cattle) which could bring the light to interrelation between AMU and farm biosecurity. In a study conducted in Belgium and Netherlands where farm biosecurity scores were compared with antimicrobial use in high-antimicrobial-consuming broiler and pig farms it was confirmed that farm-specific biosecurity strategies can contribute to decrease of lowering the risk for animal disease and therefore, the associated use of antimicrobials.[16] For the purposes of this review, we used another indicator: Human Development Index (HDI), which is, up to our knowledge, used for the first time for assessment related to the AMU, as presented in Table 2, to assess the relation between antibiotic consumption in food-producing animals and level of HDI per country. United Nations created HDI as an indicator to evaluate the level of development of a country, to emphasize that capabilities of people to achieve their full potential, life expectancy, education and income, and not only economic growth.[17] HDI data showed that five countries with the lowest recorded antibiotic consumption levels (<20 mg/PCU) in food-producing animals were also countries with a very high HDI scores (Norway, Iceland, Sweden, Finland), followed by other countries with high HDI levels (Germany, France, Belgium) where low-moderate level of AMU (≥20 ≤ 50 mg/PCU) was recorded. Interestingly, some countries with a high HDI levels (Italy, Spain) were associated with the high AMU level (≥100 mg/PCU) (Table 2). Evidently, the HDI level, as a general indicator of country development level, although helpful, can`t be always considered as an indicator for the level of AMU in food-producing animals; this should be ideally based on relation between AMU and farm biosecurity levels in country.

Apparently, in countries in which higher rate of AMU in livestock treatments has been reported, this was associated with relying of antimicrobials as a routine preventative treatment and general use of antimicrobials (including VCIA) as management tool rather than keeping them in reserve and using only when they are really needed.[18] Further, assessment of statistical links between AMU and antibiotic resistance in farm animals and antibiotic resistance in humans was carried out in a survey carried out jointly by EMA, European Centre for Disease Control (ECDC) and European Food Safety Authority (EFSA).[19] Assessment was targeted to antimicrobials licensed for use in farm food production animals and it was focused on *E. coli*, *Salmonella* and *Campylobacter*. Scarcity of data on antibiotic resistance and incosistency in reporting among countries presented a challenge for firm conclusions. However, it is encouraging to record the trend of decreased use of antimicrobials in farm food-producing animals comparing to its use in humans; this applies, in particular, to a class of antimicrobials called polymyxins (e.g. colistin) which are commonly used in healthcare settings and hospitals for treatment of multidrug-resistance infections, which use was almost halved in food producing animals. In spite of these limitations, same statistical significance was observed related to the occurrence of AMR in humans (antibiotic use in humans versus resistance in humans) and association with antibiotic use and resistance in farm animals, in particular for *Salmonella* and *Campylobacter*. On the contrary, the antibiotic resistance in humans for *E. coli* was not related to antibiotic use in farm animals, but rather to the use of antimicrobials solely in humans (in particular for aminopenicillins, 3rd and 4th generation cephalosporins and fluoroquinolones).[19]

Lastly, it should be also noted that acquiring the valid data on sales and use of veterinary antimicrobial agents at the national level requires a long-term period of time (e.g. three to four years) for assessment and the data obtained in the first years should be interpreted with a reasonable caution. This is also due to other important data needed to assess the situation properly, related to the size of national production of animals, animals` demography, registered veterinary medicinal products on the market, animal disease incidence and outbreaks, etc. Since the methodology of data collection on sales and use of veterinary antimicrobial agents is not harmonized between EU MSs it is difficult to provide direct comparison between countries.

Meat production chain and AMR

In the previous decade, the AMR associated with zoonotic food-borne pathogens was recognized as a siginificant public health concern and a global threat.[6,20–22] Further, it is also known that around 75% of newly emerging infectious diseases in humans belong to zoonotic diseases, including food-borne zoonoses.[23] The meat chain, which includes the production, processing, and distribution of meat and meat products, can be a source of AMR due to the widespread use of antimicrobials in animal agriculture. The health status of meat-producing animals (cattle, pigs, sheep, poultry), including the misuse/overuse of antimicrobials, in particular associated with intensive production systems and low level of farm biosecurity, is of critical importance for potential development and spread of AMR via food/meat consumption.[24] WHO and other public health organizations have called for the responsible use of antimicrobials in animal agriculture to help reduce the spread of AMR in humans.[24] This includes the use of alternative approaches to disease prevention and treatment, such as improved animal husbandry, farm biosecurity, vaccination, and hygiene practices. In addition, the efficient and harmonized systems for data collection on sales and use of veterinary antimicrobial agents at national level, as well as monitoring, surveillance and reporting of AMR in meat-producing animals are crucial in developing effective risk mitigation strategies for AMR, reducing of public health risk and facilitating international meat trade.

AMR occurrence and tracking in the meat chain

Tracking of AMR in the meat chain was launched officially for the first time in 1995 in Denmark which was the first country to establish a systematic and continuous, integrated monitoring programme of AMU and AMR in animals, food and humans under the umbrella of Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP). Following that, AMR monitoring programmes were established in other countries, such as Norway (Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway; NORM-Vet), Sweden (Swedish Veterinary Antimicrobial Resistance Monitoring; SVARM & Report on Swedish Antibiotic Utilisation and Resistance in Human Medicine; SWEDRES), the Netherlands (Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands; MARAN & Consumption of Antimicrobial Agents and Antimicrobial Resistance among Medically Important Bacteria in the Netherlands; NETHMAP), France (French surveillance network for antimicrobial resistance in pathogenic bacteria of animal origin; RESAPATH), the United States (National Antimicrobial Resistance Monitoring System; NARMS), Canada (Canadian Integrated Program for Antimicrobial Resistance Surveillance; CIPARS). In addition, other numerous studies linking AMR to the meat have been published addressing specific modules within the meat production chain (Table 3).

However, there are still present discrepancies related to interpolation of AMR data between European contries, as well as other aforementioned surveillance schemes and their approach related to the type and frequency of sampling, detection methods and cut-off values. For this reason, EFSA issued a manual providing guidance for reporting AMR data in food-producing animals and food of animal origin[43] with objective to harmonize reporting between the EU MSs. This should ensure that collected AMR data are relevant and easy to analyse at the EU level. The guidance covers *Salmonella* spp., *Campylobacter coli* and *Campylobacter jejuni*, MRSA, indicator commensals *Escherichia coli* and indicator *Enterococcus*, as well as the animal populations and food categories. The specific guidance is given for reporting mandatory data on *Salmonella* spp. and commensal indicator *E. coli* producers of extended-spectrum β-lactamase (ESBLs)/AmpCs/carbapenemases, obtained from the harmonized routine and specific monitoring. The most important aspects in enabling harmonized approach to AMR monitoring, surveillance and reporting are related to sampling, such as stage (farm, slaughterhouse, retail outlet), method, site (the part of a carcase, the part of the facilities for an environmental sample), sample size (in g, cm^2 or mL), information on the use of swabs or other instruments, the number of (sub) samples/sample units taken, the pooling of samples if any (refer to the number of samples combined by pooling, if available), the possible storage of samples and the length of storage (where relevant), as well as the sampling entity (competent authority, owner of animals, food business operator). The main food-producing animals should be covered (Table 4). As for the analytical methods and cut-off values, the guidance provided by the EU Reference Laboratory for antimicrobial resistance (EURL-AR) for *Salmonella*, *Campylobacter* and *E. coli* should be followed.[44]

AMR in food producing animals

Antimicrobial resistance in food-producing animals is a significant issue that poses a threat to both, animal and human health. Food-producing animals, such as livestock and poultry, are often raised in intensive farming systems where antimicrobials are frequently used for disease prevention and growth promotion, with approximately two thirds of the tonnage of antiobiotics sold intended for use in livestock for food production.[43] However, the misuse and overuse of antimicrobials in these animals contribute to the emergence and spread of AMR. There are several ways in which AMR develops in food-producing animals. Firstly, when antimicrobials are used in animal agriculture, susceptible bacteria are killed off, but a small proportion of bacteria that are naturally resistant or acquire resistance genes through mutation or horizontal gene transfer survive.[45] These resistant bacteria can then multiply and spread within animal populations. Secondly, the careless use and overuse of antimicrobials in animals, associated with inadequate withdrawal period prior placing animal-derived food on the market, can lead to the presence of antibiotic residues in animal products, such as meat, milk and eggs. The presence of antibiotic residues in the meat chain is within the scope of the national residue monitoring program; however, due to randomization of sampling it may happen that on

Table 3. Overview of studies linking AMR to the meat chain.

Authors	Type of article	Research focus	Bacterial species	Module in the meat chain				
				Farm	Abattoir	Meat processing	Retail	Consumers
Roasto et al. (2023)[25]	Review	Pork meat chain	*Salmonella enterica*	x	x	x	x	
Xedzro et al. (2023)[26]	Original research	Raw chicken, beef, pork, and wild meat	Multidrug-resistant *Escherichia coli*				x	
Habib et al. (2023)[27]	Original research	Chicken meat	ESBL- producing *Escherichia coli*				x	
de Mesquita Souza Saraiva et al. (2022)[28]	Review	Poultry meat chain	*Salmonella* spp. *Campylobacter* spp. *Enterococcus* spp. *Escherichia coli* *Staphylococcus aureus*	x	x	x	x	x
Lazo-Láscarez et al. (2021)[29]	Original research	Poultry meat chain (broiler chicken)	*Campylobacter* spp.	x	x		x	
Samtiya et al. (2022)[30]	Review	Food of animal origin (poultry/poultry meat, pigs/pork meat, catfish, raw milk, eggs) Environment	*Acinetobacter* *Enterococcus* Enterobacteriaceae ESBL- producing *Escherichia coli* *Campylobacter* *Salmonella enterica* *MRSA* *Pseudomonas* *K. pneumoniae* *S. pneumoniae*	x			x	x
Lee et al. (2022)[31]	Original research	Chicken meat chain	MRSA	x	x		x	
Igbinosa et al. (2022)[32]	Original research	Poultry meat	*Salmonella enterica*				x	
Consumption of Antimicrobial Agents and Antimicrobial Resistance among Medically Important Bacteria in the Netherlands (NETHMAP)/ Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherland (MARAN) (2022)[33]	Technical report	Meat chain (clinical samples, meat) Pigs, cattle, broilers, layers	*Salmonella enterica* (*Salmonella enteritidis, Salmonella typhimurium*) *Campylobacter (Campylobacter jejuni, Campylobacter coli)* Pathogenic *E. coli* (STEC/EPEC/aEPEC) from human patients Indicator *E. coli* from livestock, meat and vegetables *Enterobacterales* (ESBL/pAmpC/CPE/mcr) from various sources MRSA from livestock and meat	x			x	x

(*Continued*)

Table 3. (Continued).

				Module in the meat chain				
Authors	Type of article	Research focus	Bacterial species	Farm	Abattoir	Meat processing	Retail	Consumers
Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP) (2021)[34]	Technical report	Pork, cattle and poultry meat chain (clinical samples from diseased aimals and indicator bacteria from healthy food-producing animals)	*Campylobacter (Campylobacter jejuni, Campylobacter coli)* *Salmonella enterica* *(Salmonella typhimurium*, other *Salmonella* serotypes - *S. Dublin, S. Derby*) Haemolytic *Escherichia coli* WGS-based detection of resistance genes	x				x
Swedish Veterinary Antimicrobial Resistance Monitoring (SVARM)/Swedish Antibiotic Utilisation and Resistance in Human Medicine (SWEDRES) (2021)[35]	Technical report	Pork and bovine meat chain (clinical samples)	*Salmonella enterica* *(Salmonella typhimurium*, other *Salmonella* serotypes - *S. Dublin, S. Derby*) *Campylobacter* *Escherichia coli* ESBL-producing *Enterobacteriaceae* MRSA	x				x
French surveillance network for antimicrobial resistance in pathogenic bacteria of animal origin (RESAPATH) (2019)[36]	Technical report	Meat chain and pets (clinical samples from diseased animals) Cattle, sheep, goats, pigs, poultry, rabbits, fish, horses, dogs, cats	Multidrug resistance (MDR) *Escherichia coli* *Enterobacter* spp. *Klebsiella pneumoniae*	x				x
Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway (NORM-vet) (2021)[37]	Technical report	Meat chain and pets (clinical samples) Pigs, canines, turkeys, horses, bovines, felines, chickens, sheep, reindeer and goats	*Salmonella* spp. *Campylobacter* spp. *Yersinia enterocolitica* *Shigella* spp. *Escherichia coli* *Enterococcus* spp. MRSA	x				x
Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) (2020)[38]	Technical report	Meat chain Active surveillance: clinical samples from healthy cattle, pigs, chickens and turkeys & along the meat chain Passive surveillance: *Salmonella* isolates submitted to provincial or private animal health laboratories from sick or dead animals (primarily cattle, pigs, chickens, turkeys, and horses)	*Salmonella* spp. (*Salmonella Enteritidis*) *Campylobacter* spp. *Escherichia coli* *Enterococcus* *Clostridium perfringens*	x	x		x	x

(*Continued*)

Table 3. (Continued).

Authors	Type of article	Research focus	Bacterial species	Module in the meat chain				
				Farm	Abattoir	Meat processing	Retail	Consumers
US National Antimicrobial Resistance Monitoring System (NARMS) (2019)[39]	Technical report both – whole genome sequencing and antimicrobial susceptibility testing are completed	Retail meat (chicken breast, ground turkey, ground beef, shrimp, tilapia, salmon, chicken liver, chicken gizard, chicken heart)	*Salmonella* *Campylobacter* *Escherichia coli* *Enterococcus*				x	x
Päivärinta et al. (2020)[40]	Original research	Chicken (broiler) meat (caecal samples & vacuum-packed raw broiler meat)	ESBL/AmpC *Escherichia coli*		x			
Yang et al. (2020)[41]	Original research	Poultry meat	*Salmonella Enteritidis* *Salmonella Typhimurium*				x	
McNulty et al. (2016)[10]	Review	Meat chain	*Salmonella* *Campylobacter* *Enterococcus* *Escherichia coli*	x	x	x	x	x
Cameron, and McAllister (2016)[42]	Review	Beef production (bovine microbiota)	*Campylobacter* *Salmonella* *Staphylococcus aureus* *Listeria monocytogenes* *Strepotococcus spp.* *E. coli* *Enterococcus spp.*	x				

Table 4. Food-producing animals (species) and bacteria for AMR reporting.[48]

Bacteria	Animal species (food-producing animals)/Food categories
Salmonella spp.	Laying hens, broilers, fattening turkeys, fattening pigs, bovine animals under 1 year of age[(a)] Fresh meat of broilers and turkeys
Campylobacter coli/Campylobacter jejuni	Broilers, fattening turkeys[(a)], fattening pigs[(b)], bovine animals under 1 year of age[(a)]
Indicator *E. coli*	Broilers, fattening turkeys[(a)], fattening pigs, bovine animals under 1 year of age[(a)] Fresh broiler meat, fresh turkey meat, fresh pig meat and fresh bovine meat
Indicator *enterococci*[(c)]	Broilers, fattening turkeys[(a)], fattening pigs, bovine animals under 1 year of age[(a)]

(a)Where the production of turkey/bovine animals under 1 year of age meat in the EU MSs is more than 10,000 tonnes per year; (b)In fattening pigs, AMR-testing is mandatory only for *Campylobacter coli*; (c)If an EU MS decides to test for AMR in *Enterococcus faecalis* and *Enterococcus faecium* on a voluntary basis.

certain occasions antibiotic residues are found in food of animal origin. If these products are consumed by humans, they can contribute to the selection and dissemination of antibiotic-resistant bacteria in the human population.[46] Thirdly, the close proximity and high stocking densities in intensive farming systems provide an environment where bacteria can easily spread and exchange genetic material, including resistance genes. This can occur within a single animal, between animals within a farm, or between farms and other environments.[47]

The most recent EU data on AMR in zoonotic bacteria (*Salmonella* spp. and *Campylobacter jejuni and C. coli*) and indicator bacteria (ESBL-/AmpC β-lactamases (AmpC)/carbapenemases (CP)-producers - *E. coli* and MRSA) in humans, food-producing animals and derived meat, revealed that in *Salmonella* strains isolated from humans the overall high levels in resistance to ampicillin, sulfonamides and tetracyclines were observed, while very low level of resistance (1.1%) was recorded to 3rd - generation cephalosporins (cefotaxime and ceftazidime).[48] Interestingly, within the period of previous five years, certain decline is resistance to ampicillin and tetracyclines in humans was recorded, in particular in *Salmonella typhimurium* isolates which are also commonly present in calves and pigs. On the other hand, increasing trends in resistance to ciprofloxacin were observed for *S. enteritidis* which is predominantly associated with poultry and eggs.[48] For the first time, AMR data on *E. coli* isolates from meat sampled at border control posts have been presented. Similarly, the indicator *E. coli* isolates from food-producing animals and derived meat showed moderate-to-very high levels of resistance to ampicillin, sulfonamides and tetracyclines, while resistance to third-generation cephalosporins (cefotaxime and ceftazidime) was barely detected. Further, resistance to fluoroquinolones (ciprofloxacin and nalidixic acid) was high-to-very high for *Salmonella* spp. and indicator *E. coli* isolates obtained from poultry (broilers, turkeys) and poultry carcasses/meat.[48] The resistance occurrence for ESBL-/AmpC-/carbapenemase-producers in isolated *Salmonella* strains from food-producing animals and meat (broilers, laying hens, fattening turkeys, fattening pigs, as well as broilers` and fattening pigs` carcasses), as well as from indicator *E. coli* originated from food-producing animals, showed generally low levels.[48] Resistance to colistin was uncommon among *Salmonella* spp. and *E. coli* isolates recovered from food-producing animals, while resistance to amikacin, the new substance included in the harmonized panel for 2021, was very low or low in *Salmonella* spp. and *E. coli* isolates from fattening pigs, with no resistance detected in *Salmonella* spp. isolates from bovine animals under 1 year of age. The worrisome results have been obtained in resistance patterns for *C. jejuni* and *C. coli* where high to extremely high levels of resistance to fluoroquinolones, CIA for the treatment of *Campylobacter* infections in humans, have been shown in samples isolated from human (22.2% – 100%) and food-producing animals (41.7% to 80.4%). Further, multi-drug resistance was higher in *C. coli* isolated from humans, calves and fattening pigs (9.9%, 39.3% and 9.7%, respectively) while for *C. jejuni* isolated from humans and the animal species was generally low.[45] In addition, a voluntary monitoring for MRSA in EU MSs in 2021, revealed resistance to vancomycin (sheep meat) and rifampicin (pig and bovine meat); this is valuable information knowing that both antimicrobials are important in human medicine for the treatment of MRSA.[48]

Encouraging finding was that combined resistance to WHO CIA, e.g. cephalosporins and fluoroquinolones, was uncommon for indicator *E. coli* in all food-producing animals, while separate resistance levels were median for colistin, azithromycin and 3rd - generation cephalosporins.[48] It may certainly lead to reduction of the potential for horizontal transmission of resistance genes between indicator (commensal) bacteria and pathogens, in environment and food (meat) processing.

In a study carried out in nine European countries (Belgium, Bulgaria, Denmark, France, Germany, Italy, the Netherlands, Poland and Spain), in 333 poultry (conventional broiler) and pig (farrow-to-finish) farms antimicrobial resistance genes (ARG) were examined in airborne farm dust. It was observed that lower ARG levels were associated with higher farm biosecurity standards, but other factors also influenced abundance of ARG such as summer season and type of bedding materials for poultry, as well as lower animal density and summer season for pigs.[49] Such findings can be beneficial in creating effective farm management policy.

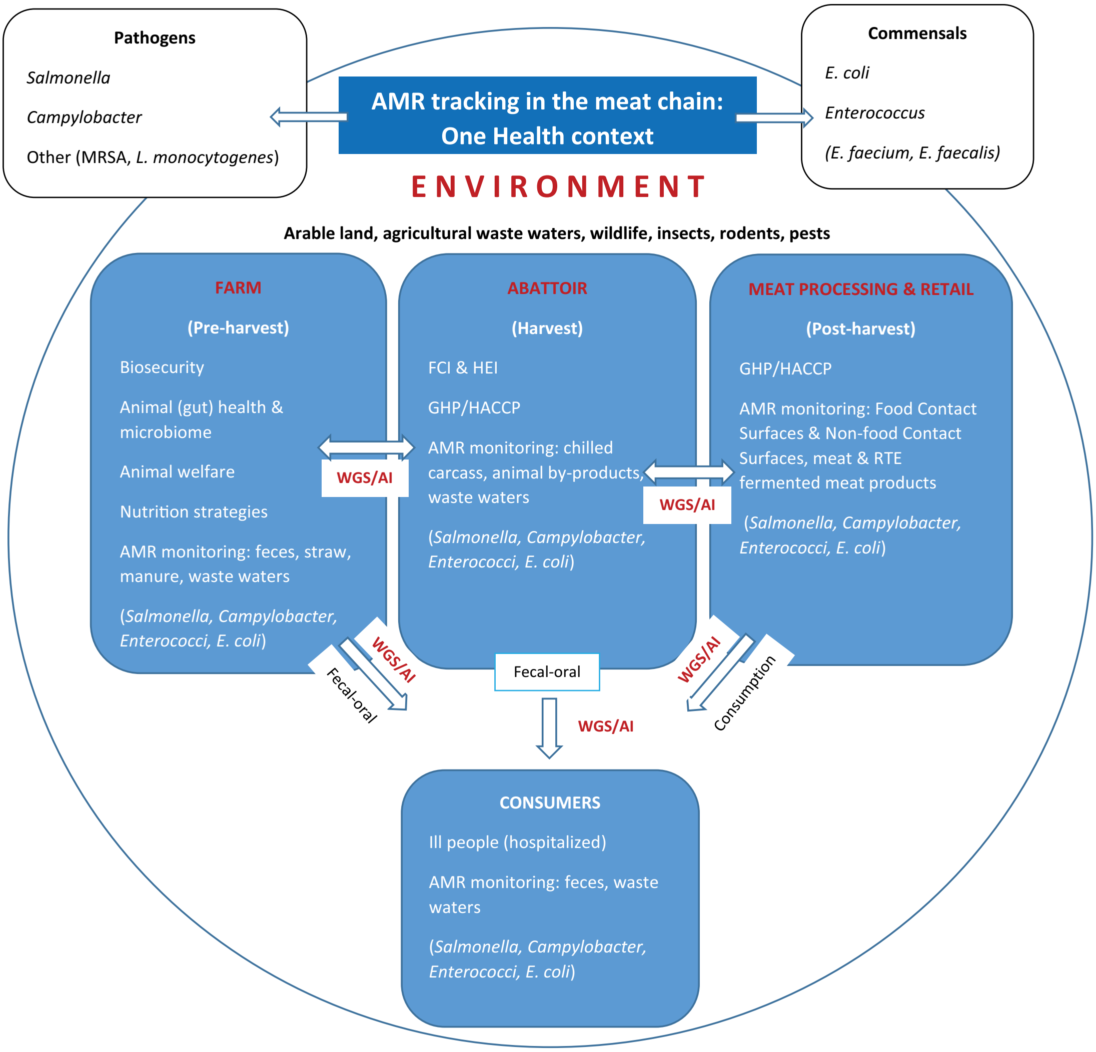
AMR in meat products

AMR related to meat products is commonly reported in raw fermented meat products, since the production process of this group of meat products doesn`t require pasteurization as a specific `kill step` and it is based on fermentation, drying and ripening process which are sometimes difficult to control precisely, so there is a potential threat that resistant pathogens can survive the technological process. Considering the link between spreading of resistant bacteria or determinants of antimicrobial resistance and production of fermented meat products, it is necessary to closely connect the entire agricultural-food chain with the breeding of domestic animals on farms and slaughtering of animals in slaughterhouses.[50,51] The ever-increasing usage of antimicrobials in the world, which has been receiving the character of overuse or even misuse in husbandry[52] has caused an uncontrolled spread of antimicrobial resistance (AMR), starting from farm-through manure-to external environment,[53] by which animal food, water and soil became directly exposed to risk, then through ready-to-eat (RTE) food themselves, as well by workers` direct contact at any stage of agricultural production[51,54] (Fig. 1).

Raw fermented meat products

Food fermentation is the oldest form of food preservation but also a cost-effective method of processing food to obtain a novel product of particular flavour, texture and colour, with enhanced nutritional, health value and digestibility as well as longer shelf life.[55] Today, there are a number of different types of fermented meat products on the global food market, based on technological parameters – type of microorganisms (already present or added), the origin of the meat used and mincing degree, additives, processing method, application or absence of fuming, ripening degree, as well as the environment itself where fermentation is carried out.[56,57]

Habitat contamination with antimicrobial drugs has a direct impact on AMR profile of commensal microorganisms such as *E. coli* and *Enterococci*[58] which can serve as carriers of AMR spreading it via directi horizontal contact with pathogens (*Salmonella*, *Campylobacter*). A direct correlation has been found between the qualitative composition of the environmental bacteria and meat, used as a raw material in the production of fermented sausages, even though the slaughtering process is carried out in controlled hygienic conditions.[59] It was observed that presence of resistant types of lactic acid bacteria (LAB) in fermented sausages is in direct correlation with microorganisms present in raw meat, as well as in other ingredients (spices and herbs) used in their production.[54,60] In addition, different types of natural casings intended for stuffing meat sausages, which contain a significant number of LAB (e.g. *Lactobacillus reuteri*, *L. plantarum*, *L. brevis* and *Lactococcus garvieae*) originating from animal intestines[54,59] can serve as a potential source of AMR genes in domestic and industrial



AMR: Antimicrobial resistance; FCI: Food Chain Information; HEI: Harmonized Epidemiological Indicators; GHP: Good Hygiene Practice; HACCP: Hazard Analysis and Critical Control Points; WGS: Whole Genome Sequencing; AI: Artificial Intelligence (machine learning)

Figure 1. AMR tracking in the meat chain.

production environment.[60] In other words, fermented meat products, obtained from the raw material containing bacteria expressing AMR, represent a vector for AMR transmission in humans.[61] It is evident that technological process in the production of raw fermented meat products carries a certain risk for cross-contamination during the production process and subsequent contamination of the RTE product itself. Thus the only possible way to reduce and control the risk of AMR bacteria transmission related to contamination of RTE fermented (raw) meat products is proper food handling based on application of good hygienic practice (GHP) and good manufacturing practices (GMP).[62] Increased demands for a larger quantity of fermented meat products, after the Second World War, have caused an intensive development and usage of starter cultures (such as LAB) in meat industry with the aim of regulating the fermentation process and standardizing production.[63] LAB have the most dominant role in the production of dry fermented sausages (especially in Europe), so their AMR patterns should be considered as a source of potential public health hazard. LAB are widely present in nature and they are common microbiota of human and animal gastrointestinal tract. European Food Safety Agency Biological Hazards Panel (EFSA BIOHAZ) issued opinion on key safety requirement of LAB used in the production of fermented products, additionally introduced criteria for mandatory absence of mobile AMR determinant in relation to certain antimicrobials, e.g. antibiotics (ampicillin, vancomycin, gentamicin, kanamycin, streptomycin, erythromycin, clindamycin, tetracycline and chloramphenicol).[64–66]

Until recently, the question of antimicrobial resistance in LAB has not been the subject of frequent investigations, unlike antimicrobial resistance in pathogenic microorganisms. To support this,[67] reported that until 1990, there were 2735 articles in scientific literature dealing with the issue of antibiotic resistance in LAB and that from that period until 2021, that number increased more than tenfold. Published results showed that LAB had a large spectrum of both intrinsic and acquired antimicrobial resistance which is directly conditioned by frequently present plasmids on which certain determinants resistant to antimicrobials can be found.[68,69] Apart from vertical transmission of antibiotic resistance determinant within the same LAB species, horizontal transmission was also established, both among LAB species and between LAB and pathogenic bacteria.[70–72]

Frequent consumption of various dry fermented meat products leads to a significant quantitative and qualitative uptake of LAB viable cells into human gastrointestinal tract, including the possibility that these microorganisms might be carriers of AMR which causes serious public health concern.[73,74] Therefore, apart from other mandatory checks of safety parameters and starter culture quality,[75] the issue of their antibiotic resistance should be properly tested before approval.[76]

Numerous examinations have shown that in dry-fermented sausages the predominant LAB species are: *Lactobacillus (L. sakei*, *L. curvatus, L. plantarum), Leuconostoc mesenteroides*, *Pediococcus pentosaceus, Lactococcus lactis*, *Streptococcus thermophilus* and *Enterococcus spp*., regardless of whether the sausages are produced in industrial or entrepreneurial (domestic) conditions. In comparison with EFSA opinion, all mentioned microorganism species, except *Enterococcus* spp., have Qualified Presumption of Safety (QPS) status which is carried out by EFSA BIOHAZ as generic pre-evaluation to support safety risk assessments of biological agents intentionally introduced into the food and feed chain.[54,77–80] Moreover, as majority of LAB strains isolated from food have acquired antibiotic resistance along the food production chain, their further potential application should also include checking of this issue, including the probiotics used in animal farming systems that can be carriers of resistance genes for the human gut microbiota when consuming either improperly cooked animal-derived food or, for example, raw (fermented) meat products.[81–83]

The first step in studying LAB antibiotic resistance is related with their coded intrinsic (non-horizontally transferable) resistance reported to bacitracin, vancomycin, kanamycin and β-lactams, to be able to assess the acquired resistance modes to common antimicrobials in the next phase. As one of the first findings in this field, the high natural resistance to vancomycin of lactobacilli, pediococci and *Leuconostoc* spp. was found, which was very significant for distinguishing these LAB species from other gram-positive bacteria.[84] In addition, although most lactobacilli are sensitive to chloramphenicol, erythromycin, clindamycin, tetracycline and penicillin G,[85,86] this does not apply to some lactobacilli (*L. brevis, L. fermentum and L. paracasei* subsp. *paracasei)* isolated from meat and fermented sausages which have natural resistance to afore mentioned antimicrobials. Such LAB can be therefore the potential source of AMR transmission to humans via consumption of RTE fermented meat products. It requires additional precaution and assessment regarding their QPS status for usage in technological process for manufacturing fermented meat products.

The most commonly identified genes of acquired lactobacilli resistance isolated from dry-fermented sausages, coding the creation of protective proteins responsible for resistance to tetracycline are: tet(M), tet(W), tet(S), and erm(B), and erm(C) for erythromycin resistance.[50,54,87] Very often, genes encoding resistance to tetracycline and erythromycin can be genetically linked. Simultaneous presence of the genes tet(M)and erm(B) was found in *L. paracasei*,[88] *L.plantarum* and *L. salivarius*.[89] Predominant species of lactobacilli in relation to dry-fermented sausages (*L. sakei* and, especially, *L. plantarum)* have shown a high level of resistance in relation to tetracycline ranging from 12–70% and 75–80%, respectively.[90,91]

The genus *Pediococcus*, along with *Lactobacillus* spp. and *Leuconostoc* spp., have intrinsic resistance to vancomycin,[92] as well as to the effect of ciprofloxacine, trimethoprim and sulfamethoxazole.[93] Research by Imperial et al.[83] showed that all *Pd. pentosaceus* isolates ($n = 9$), isolated from fermented sausages, showed resistance (100%) to the effect of streptomycin, gentamicin, tetracycline, ampicillin, whereas resistance to chloramphenicol was 98%, to erithromycin 33%, and to clyndamycin11%. The same authors proved the presence of antibiotic-resistant genes for tetracycline – tet(M) and for erythromycin – erm(B).

Apart from LAB species, some coagulase-negative staphylococci (*Staphylococcus xylosus* and *Staphylococcus carnosus*) play a significant role in biochemical processes contributing to the specific flavour and colour of fermented sausages,[94] due to which these have been used as part of starter cultures since 1950 in fermented sausage production.[95] So far, there have not been many published results on their AMR, although most *S. xylosus* isolates have been found to be tetracycline-resistant,[96,97] whereby the AMR transmission rate among strains was very low.[98] In relation to *S. xylosus*, the rate of AMR *S. carnosus* was lower.[99]

Unlike other LAB species, enterococci did not acquire the US Food and Drug Administration (FDA) – based categorization of GRAS (Generally Recognized as Safe) status, since *E. faecalis* and *E. faecium* were recognized as opportunistic pathogens. However, their presence in dry fermented sausages cannot be exclusively viewed from the aspect of production process hygiene quality, considering that these thermally unstable microorganisms contribute to sensory properties as well as to the safety enhancement and expansion of the product shelf life.[50,100] Enterococci usually have natural resistance to low concentrations of aminoglycoside and β-lactam antimicrobials (antibiotics), quinolones,[101] as well as to the effect of cephalosporin, sulphonamide, and to a certain degree, to the effect of clindamycin.[54,75] Acquired resistance exists to chloramphenicol, erythromycin, clindamycin, aminoglycosides, tetracycline, ß-lactams, fluoroquinolones and glycopeptides.[102] Importantly, enterococci resistant to vancomycin are of extreme importance in the food (meat) chain, since this antibiotic is used in treatment of many bacterial infections including those by enterococci, as well as the infections caused by methicillin-resistant *Staphylococcus aureus*. Although the prevalence of these enterococci is not high, transfer of vancomycin resistance determinant *van* (A) *E. faecalis* to other non-pathogenic bacteria takes place most commonly during the sausage fermentation process.[103,104]

Similar situation was also found in the case of their AMR in relation to tetracycline. Resistance determinants, *tet*(M), *tet*(L) and *tet*(S), found in enterococci originating from food were identical to the determinants isolated from the clinical isolates of enterococci.[105] Very often, isolates of tetracycline-resistant enterococci show resistance to erythromycin or/ and chloramphenicol as well,[106] which is related to the fact that certain *tet* genes are linked to mobile plasmids or transposons that are carriers of the resistance gene for other antimicrobials as well.[107] Since enterococci can significantly affect the AMR rate of other microorganisms, due to which the possibility of AMR animal microbiota transmission into human gastrointestinal tract increases, the presence of enterococci in thermally untreated products, such as dry (raw) fermented sausages, causes justified health concern.[108]

The afore mentioned findings point that, in addition to obtaining detailed information on LAB features, which determine their further technological application in food industry (e.g. QPS status), it is necessary to conduct adequate risk assessment that include the issue of AMR in vitro and in vivo, i.e. natural and acquired antimicrobial resistances, along with its LAB distribution from different sources,[109] regardless of whether it is traditional or industrial-based food.

AMR sampling schemes, susceptibility testing, clinical resistance and epidemiological cut-off values

AMR patterns in Europe have variations between the EU MSs and EEA countries depending on the bacterium (pathogen), antimicrobial group and geographical region.[110] These variations are present due to the lack of uniformity in sampling schemes, differences in laboratory methods used for identification of AMR profiles, different approach to clinical breakpoints (clinical resistance) and epidemiological cut-off values (microbiological resistance), including set up priorities related to public health goals. To overcome this, the `Zoonoses Directive` was introduced in 2003[13] to provide the basis for harmonization of national monitoring, surveillance and reporting system for zoonotic food borne pathogens and AMR between MSs. Up to time of writing this article, the lack of harmonization in implementation of national AMR monitoring and surveillance systems is still ongoing issue which create certain discrepancies in interpreting and extrapolating data between MSs.

As stated above, increase of AMR in humans is also in connection with misuse/overuse of antimicrobials in other ecological compartment – food producing animals. Therefore, the need for enhanced monitoring of AMR in bacteria originated from food producing animals and food of animal origin has been set out in the Commission Decision 2013/652/EU.[111] The database on AMR in food producing animals and derived food was established with particular focus on poultry flocks/poultry meat, fattening pigs and calves and derived meat.[110]

Sampling schemes

AMR sampling schemes at national level are carried out in food producing animals (cattle, pigs and poultry) and derived meat, usually sampled at the farm or abattoir. To facilitate the harmonization between the EU MSs, the EU Commission issued guidelines (e.g., target number of isolates per animal population and per slaughterhouse), method of susceptibility testing, and panel of antimicrobials and tests to be included.[111,112] Such approach aimed to improve the comparability of the data generated among MSs. The sampling is based on isolates from clinical samples regularly submitted to a diagnostic laboratory or actively collected samples from healthy or diseased animals, meat and meat products in all stages along the meat production chain: 1) pre-harvest (farm), 2) harvest (abattoir) and 3) post-harvest (retail).[112] It is important to note that the selection of isolates from clinical infections at farm level is usually done by the local veterinarian, while sampling at abattoir and retail is related to the competent authority visits (veterinary or public health inspection) in accordance with the national plan for AMR monitoring and surveillance.

Pre-harvest (farm). The minimum of 170 representative isolates of *Salmonella* spp. from laying hen flocks, broiler flocks and fattening turkey flocks should be collected and tested for antimicrobial susceptibility at annual level in each MSs. The sampling should be done either by the Competent Authority (CA) or by food business operator (FBO), under supervision by CA. In addition, population of laying hen flocks, broiler flocks and fattening turkey flocks which are monitored under the *Salmonella* National Control Programme (NCP) are also eligible for AMR Monitoring regarding *Salmonella* spp.[112] Two sampling approaches are implemented: (i) stratified sampling (proportional allocation of samples within a sampling frame of *Salmonella* spp. strains from the isolate collections available at official laboratories and/or other laboratories designated by the CA to carry out testing under the NCP requirements and (ii) simple random sampling (SRS) which includes the sampling of the population of flocks within NCP and which have already tested positive for *Salmonella*. It is advised that a quarterly SRS plan should be designed and applied in flocks tested positive for *Salmonella*.[112]

Harvest (abattoir). A minimum of 170 representative isolates of *Salmonella* spp. obtained respectively from carcasses of broilers, fattening turkeys, fattening pigs and bovines under one year of age should be collected and tested for antimicrobial susceptibility at annual level in each MS.[112]

Collection of representative cecal samples (the number to be determined according to the national production volume at annual level) should be carried out to obtain the following isolates: *E. coli* (broilers, fattening turkeys, fattening pigs and bovines under one year of age); *Campylobacter jejuni* (broilers and fattening turkeys); and ESBL-/AmpC-/carbapenemase-producing *E. coli* (broilers, fattening turkeys, fattening pigs and bovines under one year of age). The isolates of *E. faecium* and *E. faecalis* (indicator organisms) may be also taken, under voluntary basis, from broilers, fattening turkeys, fattening pigs and bovines under one year of age, including isolates of *Campylobacter coli* from broilers and fattening pigs.[112]

Post-harvest (retail meat). A minimum of 300 representative random samples of fresh broiler, pig and bovine meat should be taken at retail (outlets/supermarkets, specialist shops and markets, but excluding catering activities, restaurants and wholesalers) on annual level in each MS and tested for the presence of ESBL-/AmpC-/carbapenemase-producing isolates of *E. coli*; alternatively, a minimum of 150 samples should be collected in MS with the lower level of meat production at annual level (i.e. less than 100 000 tonnes of pig meat slaughtered per year and less than 50 000 tonnes bovine meat slaughtered per year).[112]

Antimicrobial susceptibility testing. A drug potency against specific pathogenic bacteria is quantified by susceptibility testing. This helps in establishing the formulation of the drug being a viable option for therapeutic treatments and monitoring changes related to AMR. By definition, a "s*usceptible*" means that the microorganism is susceptible to the therapy and that success when this specific antimicrobial agent is used is high. Furthermore, the effectiveness of antimicrobial drug against a specific pathogen is related to the site of infection, ability of antimicrobial to reach infection site, as well as formulations available and dosage regimes.[110]

There are two, widely accepted, methods for antimicrobial susceptibility testing (AST): Disk diffusion test and dilution method. Disk diffusion is the oldest approach and is the most widely used AST method in routing clinical testing. It is very suitable for application and almost all antimicrobial agents can be tested since it requires no special equipment.[113] The European Committee on Antimicrobial Resistance Testing (EUCAST) recommended that Inhibition zone diameters (IZD) is expressed in mm to show the minimum inhibitory concentration (MIC) breakpoints.[114] MIC identifies the minimum concentration required by an antimicrobial to inhibit the growth of an organism visually, after an overnight incubation period. It is the most widely used method for AST in clinical laboratories throughout the EU/EEA.[114] The disk diffusion method is widely used in France (RESAPATH) and Sweden (SVARM). Alternative method for AST is the dilution method (micro-broth dilution) where MIC is determined in mg/L, being a more accurate measurement than disk diffusion and is considered as a \`gold standard\` for AST. A good to excellent correlation between the values obtained in mm and in mg/L has been also observed. The (micro) dilution method is therefore recommended as the more accurate and preferred testing method. In Europe, it is widely used in Danish (DANMAP), Dutch (MARAN), Norwegian (NORM-VET),[114] as well as in Canada (CIPARS)[115] and USA (NARMS)[116] national monitoring systems for antimicrobial resistance.

Clinical breakpoints

Clinical breakpoints serve to determine therapeutic value of antimicrobials against new and already developed drugs by assessing drug potency required to inhibit or kill a pathogen within the body. Bacteria are graded in testing as follows: susceptible (s) micro-organism is defined as susceptible by a level of antimicrobial activity associated with a a high likelihood of therapeutic success using a standard dosing regimen of the agent; intermediate (I) level of antimicrobial agent activity is associated with a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection; and resistant (R) level of antimicrobial activity associated with a high likelihood of therapeutic failure even when there is increased exposure. For example, for a breakpoint listed as S ≤1 mg/L and *R* >8 mg/L the intermediate category is 2–8 (technically >1–8) mg/L.[117]

Epidemiological Cut-Off values (ECOFFs)

The EU Reference Laboratory for Antimicrobial Resistance (EURL-AR) defined standardised epidemiological cut off values (ECOFFs) needed for the comparison of antimicrobial susceptibility monitoring results.[118] Therefore, EURL-AR recommended the use of ECOFFs which categorize bacteria as follows: (i) wild type (species with the absence of acquired and mutational resistance mechanisms to the drug in question) or (ii) non-wild type (species with the presence of an acquired or mutational resistance mechanism to the drug in question). In addition, a certain number of isolates from a wild-type population is tested against ECOFFs to ensure that an identified organism can be treated to determine the likelihood of therapeutic success or failure of a specific antimicrobial for clinical purposes. Lastly, ECOFFs recommended by the EURL-AR for interpretation of AST results are defined for *Salmonella* spp., *Campylobacter coli*, *Campylobacter jejuni*, *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecium* and *E. faecalis*.[118]

Novel methods and data processing in tracking AMR along the meat chain

Whole Genome Sequencing (WGS) is a novel method that has emerged as a powerful tool for tracking food borne pathogens, as well as AMR along the food (meat) chain. WGS allows for the complete sequencing of an organism's genome, providing detailed information about its genetic makeup, including resistance genes and mutations associated with AMR.[119] By utilizing WGS, researchers can investigate the genetic profiles of bacteria found in animals, meat products, and the environment throughout the meat chain. For example, in a study carried out in Serbia,[120] WGS was used as a food safety management tool to detect entry routes of *Listeria monocytogenes* in meat processing environment (food contact and non-food contact surfaces), as well as its distribution patterns within the plant, providing valuable information on the level of risk for cross-contamination of RTE meat products.

In a study conducted in Austria researchers provided insight into bacterial community structure throughout a pork-processing plant by investigating what proportion of bacteria on meat are presumptively not animal-associated and are therefore transferred during cutting via personnel, equipment, machines, or the slaughter environment.[121] The advancement in WGS technology also enables the identification and tracking of specific strains of antibiotic-resistant bacteria, as well as the determination of their relatedness and potential transmission routes in the food chain. This is essential to identify control and prevention strategies to combat the increasing global threat of AMR.[122] In other study carried out in the United Kingdom the application of WGS in tracking the spread of MRSA in the pork production chain has been demonstrated. The study utilized WGS to compare MRSA isolates obtained from nasal and ear skin swabs of batches of pigs at slaughter and at different stages along the slaughter line (lairage – ear swab only; immediately post-stun – ear and nasal swab; and in the chiller – ear and nasal swab), revealing transmission routes and identifying potential intervention points.[123] A review on WGS application to study *Salmonella Typhimurium* strains isolated from pigs and pork products in Portugal has been done.[124] The study demonstrated the potential of WGS to elucidate the dynamics of AMR distribution between animals, the meat processing environment, and retail meat products and elaborated on transmission of pig-related multidrug-resistant *Salmonella* serotypes, clones and/or genetic elements carrying clinically-relevant antibiotic resistance genes from pigs and pork meat to humans. The transmission of ESBL-producing *Escherichia coli* in the poultry production chain was investigated in a study carried out in Ghana with the aim to investigate poultry production-food-consumer chain as a potential AMR transmission route. The study employed WGS to compare isolates from the intestinal tract of poultry (samples of faecal droppings) at farms in rural Ghana and humans (hospitalized children), enabling the identification of shared resistance genes and the tracing of transmission routes, as well as pointing out that the ESBL-producing *Escherichia coli* in sub-Saharan Africa is a serious public health concern.[125] In other study done in Italy, carried out WGS analysis of virulence and AMR genes in ESBL-producing *Escherichia coli* from samples taken from healthy animals and farm environment in four swine farms.[126] They confirmed the phenotypic antibotic resistance and virulence (enterotoxin) genes such as *astA*, *ltcA* and *stb* in ESBL-producing *Escherichia coli*. These findings highlighted the need to monitor commensal *E. coli* from healthy pigs in One Health context.

Further, emerged technologies, i.e. Artificial Intelligence (AI) are already becoming integral component of AMR monitoring, surveillance and reporting schemes enabling efficient processing of WGS-acquired data. For example, in a study carried out in China, ten large-scale chicken farms connected with four poultry abattoirs in three provinces, were monitored over 2.5 years by analyzing and comparing microbiomes from chickens, derived carcasses and environments; 145 antibiotic resistance genes (ARGs) were identified shared between chickens and environments in all farms. In this study, AI was effectively used (e.g. data mining approach based on machine learning) to analyze collected samples of microbiome and compare them for similarity between chickens, carcasses and environment.[127] Similarly, in other long-term study, also carried out in China, the MRSA isolates collected from food, as well as from healthy and hospitalized individuals over 9 years and from 27 provinces were analyzed using machine learning to reconstruct the phylogeny of the isolates and compare them to references from other countries; joint genetic traits between MRSA food isolates and humans were revealed.[128]

These studies highlight the use of WGS as an effective tool for investigating AMR along the meat chain, providing insights into the genetic relatedness and transmission dynamics of resistant bacteria. WGS enables a more comprehensive understanding of AMR facilitating the development of targeted interventions to reduce its spread and impact on public health.

WGS is a tool that will revolutionize the way how we control food safety enabling unparallaled depth of genetic information with a level of precision that was not previously possible. It allows rapid and reliable detection, identification and characterization of food borne pathogens, including their AMR patterns, along food (meat) chain and in food borne outbreaks, thus enabling reduction of risks to animal and public health.[129] It enables a new level of precision to the epidemiological and food safety surveillance along the food chain leading to faster and more efficient decision making in the preparedness and response to foodborne infections. Overall, the WGS technology, in connection with AI (machine learning for data processing), opens new possibilities and offers benefits to the food (meat) industry in a farm-to-fork continuum based on the prospects of metagenomic sequencing applied directly to the sample specimen, with or without pre-enrichment culture.[130] The regular application of WGS in food safety management can facilitate the integration of information from other sectors, such as environment, food-producing animals, food of animal origin and humans within One Health context. This can also enhance consumer protection through food and nutrition security and facilitate international food trade.[119]

International strategies and action plans on AMR

AMR has been recognized as a global health concern that affects both human and animal populations. The food chain, including the production, processing, and consumption of food, plays a significant role in the spread of antimicrobial-resistant bacteria. To address this issue, various international initiatives have been established to tackle AMR in the food chain. These initiatives emphasize the need for a holistic and multi-sectoral approach along the food chain. They promote responsible use of antimicrobials, surveillance of resistance patterns, capacity building, and international collaboration to mitigate the risks posed by AMR.

Codex Alimentarius Commission (CAC)

As an international food standards-setting body, established jointly by UN FAO/WHO, develops science-based guidelines and codes of practice to ensure food safety. It addresses AMR through its various committees and promotes responsible use of antimicrobials in food production, such as *Codex Alimentarius* Committee on Residues of Veterinary Drugs in Foods (CCRVDF) which developed the Code of Practice to Minimize and Contain Antimicrobial Resistance in 2005.[131] In 2006, the Codex established a first Intergovernmental Task Force on Antimicrobial Resistance to develop science-based guidance on assessing and managing the risks to human health associated with the presence in food and feed of antimicrobial resistant microorganisms.[132]

WHO

Leads global efforts to combat AMR, including its spread through the food chain. It has developed a Global Action Plan on AMR (GAP-AMR)[6] that emphasizes the responsible use of antimicrobials in food-producing animals and encourages the adoption of good agricultural practices based on five objectives: (i) Improve awareness and understanding of AMR through effective communication, education and training, (ii) Strengthen the knowledge and evidence base through surveillance and research, (iii) Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures, (iv) Optimize the use of antimicrobial medicines in human and animal health, and (v) Develop the economic case for sustainable investment based on needs of countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions. WHO also established Global Antimicrobial Resistance Surveillance System (GLASS) as a collaborative effort to improve global surveillance of AMR. It facilitates the collection, analysis, and sharing of data on antimicrobial resistance, including its occurrence in the food chain. Beforehand, WHO developed the categorization of antimicrobial agents based on their importance in treating human disease and advocates the prudent and justified usage of CIA in agro-food chain and humans.[24]

FAO

Collaborates with the WHO and other stakeholders to address AMR in the food chain. FAO promotes the prudent and responsible use of antimicrobials in agriculture, animal husbandry, and aquaculture through guidelines, capacity-building programs, and awareness campaigns. Since 2018, FAO, WOAH and WHO established a Tripartite body with a special focus on tackling AMR from the One Health approach. The Tripartite body became formally a Quadripartite by welcoming the United Nations Environment Programme (UNEP) to advance the coordinated strategy on human, animal and ecosystem health via AMR Multi-Stakeholder Partnership Platform as a `whole of UN approach`.[133] The Quadripartite body aims to preserve antimicrobial efficacy and ensure proper access to antimicrobials for responsible and prudent use in human, animal and plant health, as well as to contribute to the UN Sustainable Development Goals (SDGs) and the implementation of the GAP-AMR. Further, FAO launched its Action Plan on Antimicrobial Resistance 2021–2025, serving as a roadmap for focusing global efforts to address AMR in the food and agriculture sector.[134] FAO also established the Joint FAO/WHO Centre for Zoonotic Diseases and AMR (CJWZ) aiming to coordinate the FAO's work on AMR within the context of the FAO AMR Action Plan. The joint centre aims to coordinate, build up policy and strategy, publish knowledge products, scientific advice, communication, and support project implementation. The newest development is related to FAO RENOFARM (Reduce the Need for Antimicrobials on Farms) initiative. RENOFARM is a global project that applies to the whole production chain aiming to raise awareness of the need to reduce antimicrobials in the worldwide agrifood systems. RENOFARM liaises with the FAO `Hand-in-Hand (HIH) Initiative`, supporting the implementation of nationally led, ambitious programs to accelerate agro-food systems transformations by fulfilling UN SDGs, such as eradicating poverty (SDG1), ending hunger and malnutrition (SDG2), and reducing inequalities (SDG10). RENOFARM aims to make farms more sustainable by introducing or improving best practices, health and vaccination programs, biosecurity measures, and antimicrobial alternatives.[135]

WOAH

Focuses on animal health and welfare and works to prevent the emergence and spread of AMR in animals. It provides guidelines and standards for the responsible use of antimicrobials in veterinary medicine (i.e. VCIA) and promotes surveillance of AMR in animal populations. WOAH launched its strategy on Antimicrobial Resistance[136] in 2016, aligned with the WHO GAP-AMR.[6] The strategy recognizes the importance of a "One Health" approach involving human and animal health, and agricultural and environmental needs. It encourages the national implementation of international Standards.

Other UN AMR initiatives

The Declaration of a High-level Meeting of the UN General Assembly on Antimicrobial Resistance in 2016 has also represented an important step in the world's commitment to tackle AMR.[137] The declaration called for greater and more urgent actions in response to AMR. An interagency coordination group (IACG) composed of WHO, FAO and WOAH was established to provide practical guidance for approaches needed to ensure sustained, effective global action to address AMR. IACG issued a report to the UN Secretary-General titled "No time to wait: securing the future from drug-resistant infections" calling for accelerating progress in all countries, innovation to secure the future, effective collaboration, more investment for sustainability, strengthening accountability and global governance.[138]

European one health action plan against AMR

The European Union (EU) has implemented various initiatives to combat AMR and in 2013 introduced the regulation on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria.[139] The impact on the food chain is also addressed by EARS-Net which is the largest publicly funded system for AMR surveillance. These efforts involve increasing public awareness on AMR, promoting prudent use of antimicrobials in agriculture, improving evidence through monitoring and surveillance programmes, better prevention and control, better adherence to EU rules to tackle AMR, and supporting research and innovation. The special emphasis has been put on environment, which is recognized as a contributor to the development and spread of AMR in humans and animals, in particular in high-risk areas due to human, animal and food processing waste streams. The EU Guidelines for the prudent use of antimicrobials in veterinary medicine along with Guidelines for the prudent use of antimicrobials in human health have been issued by the European Commission.[140,141]

The indicators should be developed to help MSs to measure the performance of their One Health Action Plans on AMR and reduce infections by key resistant microorganisms (e.g. *Campylobacter*, *Salmonella*) in humans and food-producing animals, to improve the adeqate and prudent use of antimicrobials in the human and veterinary sectors.[142] The EU Commission identified AMR as one of the top three priority public health threats, in 2022. This was followed by proposal to combat AMR in One Health approach where the importance of the environment in development and spread of AMR is recognized, together with contribution of globalized markets and the growing movement of people, animals, plants and derived products to the spread of AMR.[143] The importance of development and introduction of novel and effective antimicrobials (e.g. antimicrobial peptides) is recognized to overcome the existing and increasing resistance of microorganisms to available drugs.[144] For example, introduction of antimicrobial peptides can be a solution for replacing `traditional` antimicrobials needed to maintain gut health and immunological status of livestock, since these peptides can eliminate bacterial population, improve immunity by restoring intestinal epithelium, thus providing therapeutic effect on piglet diarrhea, reducing inflammation and even enabling biofilm destruction.[145–148]

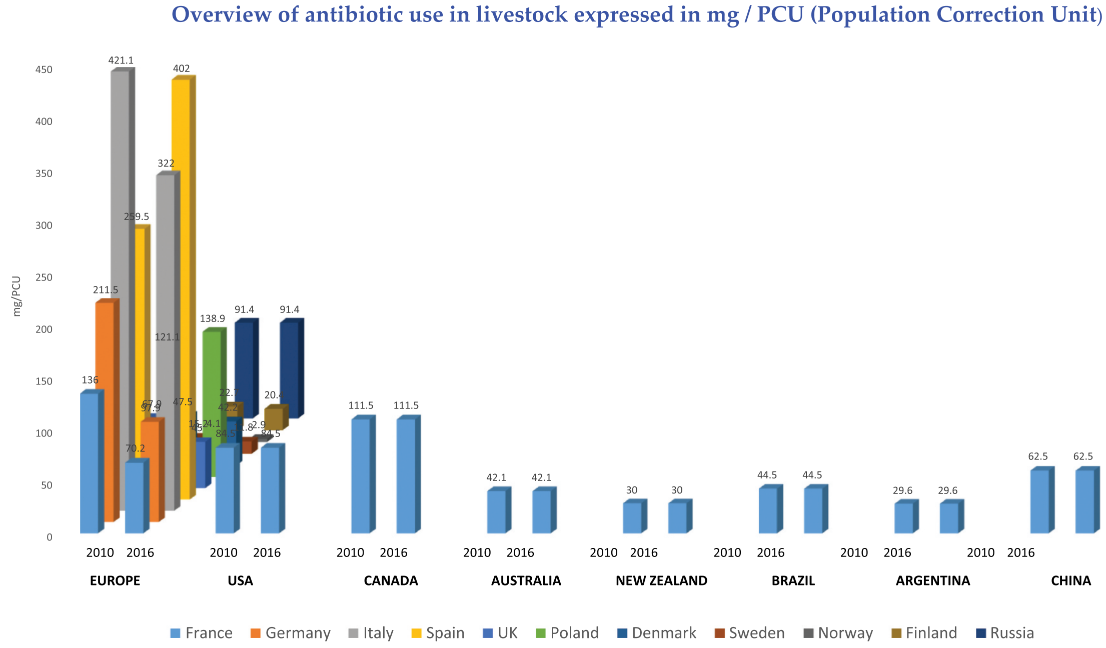


Figure 2. Overview of antibiotic use in livestock.[145–147]

Table 5. Antimicrobial consumption in food producing animals and humans in EU/EEA countries, in 2017.[149]

	Antimicrobial consumption (mg/kg estimated biomass)	
Antimicrobial agent	Food producing animals	Humans
Tetracyclines	0.05–173.5	0.2–11.7
Aminopenicillins	0.1–78.3	7.3–128.8
Macrolides	0–22.0	1.2–18.0
Fluoroquinolones and other quinolones	<0.01–15.3	2.2–24.0
Polymyxins (including colistin)	0–14.9	0–0.2
Third- and fourth-generation cephalosporins	<0.01–0.8	0.1–11.4
Total consumption	**3.1–423.1**	**52.8–212.6**

The afore mentioned initiatives are in line with increased awareness on antibiotic use in livestock in the EU, starting more than one decade ago.

Apparently, the overall antibiotic use in meat (food) producing animals has decreased over time, comparing to some regions (e.g. US and Canada) in the world (Figure 2), which is encouraging. The overall use of antimicrobials in food-producing animals in the EU became lower than in humans. It means that measures that have been taken at national level of MSs were effective, observed with noted decrease in the use of VCIA, such as macrolides, fluoroquinolones, polymyxins (including colistin) and 3rd- and 4th generation cephalosporins in livestock within the period 2016–2018. This is very promising, in particular, since polymyxins are used in hospitals as a therapeutic choice to treat patients infected with multi-drug resistant bacteria.[149] In addition, the use of tetracyclines and aminopenicillins should be substantially reduced in food producing animals, with necessary precautions to avoid deterioration of animal health in intensive livestock farming systems. An overview of antimicrobial consumption in food producing animals and humans in EU/EEA countries is given in Table 5.

However, it is noted that not all EU MSs succeeded to achieve the goal to substantially reduce the antimicrobial use in livestock. For example, Spain even increased the use of antimicrobials within the six years` period of time (i.e. 2010–2016), while Italy still preserved relatively high level of usage of antimicrobials in livestock, although slightly reduced within the same period of time.[145] This could be attributed to economic factors (striving for improved animal health and increased productivity), lack of alternatives (feeding management, vaccination, housing conditions), limited awareness (lack of outreach programs to inform farmers about the importance of reducing antimicrobial use and the benefits of alternative practices), regulatory aspects (differences between EU MSs in AMR monitoring and reporting), intensive farming practices (high stocking density on farm can increase the risk of disease transmission and might necessitate the use of antimicrobials to control outbreaks), global market pressures (competitiveness and concerns about reduced productivity and increased costs associated with reducing antimicrobial use) and resistance to change (entrenched practices, lack of motivation to adapt, or reluctance to try new methods). The pathway for improvement of livestock farming practices and reduction of antimicrobial use is related to development of resources and expertise to implement alternative practices to antimicrobial use, as well as communication and collaboration between key stakeholders based on One Health context (government agencies, farmers, veterinarians, researchers and consumers.) On the other hand, Denmark, Sweden and Finland reduced, already low level, the usage of antimicrobials to even lower levels and remain the most successful countries with the lowest rate of antibiotic use in livestock farming on a global scale.

Federation of Veterinarians of Europe (FVE)

Represents around 300 000 veterinarians across 38 European countries, is an official stakeholder at the EU Institutions and aims to enhance animal health, animal welfare, public health and the protection of the environment by promoting the veterinary profession. One of the FVE core tasks is the promotion of responsible use of VMPs. Along with the EC, the Heads of Medicines Agencies, FVE and some Member States and veterinary organisations started to issue AMR strategies and/or action plans already from 2010.[148,150,151] This included a survey of European veterinary surgeons to establish their antibiotic prescribing habits and factors influencing these. The survey outcomes gave an insight into which antimicrobials were most likely used for the most common indications in different species.[152] Other FVE activities included the contribution to the EMA and EFSA joint scientific opinion (‘RONAFA’ opinion) on measures to reduce the need to use antimicrobial agents in animal husbandry in the EU and the resulting impacts on food safety suggesting an integrated approach between the local livestock production system and all stakeholders[153] or participation in drafting the new EU Veterinary Medicines Regulation[154] aiming to achieve objectives of the “Farm to Fork Strategy” and ambition to reduce the antibiotic use by 50% by 2030. Veterinarians, as gatekeepers of animal health, animal welfare and public health, and prudent and responsible use of medicines in animals are crucial in the fight against AMR. In line with this approach, FVE also joined the European Platform for the Responsible Use of Medicines in Animals (EPRUMA platform) and the AMR Stakeholder Network. FVE enact the principle of “prevention is better than cure” and “as little as possible, as much as necessary” aiming to improve animal health by other means rather than treatment. Lastly, the FVE is striving on enhancing the One Health approach on AMR prevention and control by working with the Standing Committee of European Doctors (CPME) strenghtening its commitment to fight against AMR.

US National Antimicrobial Resistance Monitoring System (NARMS)

It is an inter-agency, collaborative partnership with state and local public health and livestock/meat industry departments, based on tripartite participation of FDA, Centers for Disease Control and Prevention (CDC) and the US Department for Agriculture (USDA).[155] This surveillance system is designed to track changes in antimicrobial susceptibility of select food borne bacteria of public health importance isolated from ill people (CDC), retail meats (FDA) and food animals (USDA) by collecting specimens from two sampling points: intestinal (caecal content) and carcass or food commodity samples. The primary objective is threefold: (i) dissemination of timely information on AMR to promote interventions which will reduce resistance among food borne bacteria, (ii) research to improve knowledge on emergence, persistance and spread of AMR, and (iii) provision of data to assist FDA in approval of effective antimicrobials intended for animals.[155]

One health approach

One Health entails a multidisciplinary healthcare approach to the health of humans, animals and of ecosystems. Everyone's health and the health of the environment are interlinked.[156] One Health is officially recognized as a relevant strategy that can benefit all sectors from food systems, to animal health and welfare, to soil, forestry and to the ecosystems up to human health and wealth.[157] The protection of human health is based on proper prevention and treatment of disease in animals (e.g. zoonotic pathogens of bacterial, viral, fungal origin, including parasitic diseases and prions). The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic demonstrated the close connection between humans, animals, and the shared environment and highlighted the need for a true implementation of the One Health approach. For this reason, the availability of antimicrobials for animals is equally important for animals as it is for human health. Following this direction, four global partners, FAO, WOAH, UNEP and WHO established the interdisciplinary One Health High-Level Expert Panel (OHHLEP) to enhance their cross-sectoral collaboration.[158,159] European Institutions are committed to devoting billions of euros to the necessary research and innovation (R&I) to support a transition to safe and sustainable food systems via One Health approach.

Such example is also given in a study carried out in France,[160] where the major drawbacks and limitations in providing the platform which will foster harmonization in AMR monitoring, surveillance and reporting were considered, as follows: (i) lack of structured national surveillance programmes in the environmental sector, (ii) antibiotic residues only routinely monitored in surface water and animal-derived food (mostly meat), (iii) AMR monitoring and surveillance in the human sector mostly targets clinical samples, and rarely screening samples, (iv) lack of a dedicated AMU-surveillance programme in companion animals, (v) lack of AMR surveillance in non-captive wild animals and aquaculture, and (vi) lack of AMR testing in diseased animals to antimicrobials of primary interest in human health (e.g. carbapenems), since routine testing is limited to antimicrobials authorized in veterinary medicine. It is concluded that countries need to develop One Health surveillance of AMR by integrating data from surveillance in animals, humans, food and environment. From recently, EU Agencies agreed to strengthen their collaboration and make a difference in supporting the European research agenda by moving towards a One Health (OH) approach in design of risk mitigation strategies to address AMR.[161]

Conclusions

The AMR in the meat chain in One Health context refers to the mutual relationship between antimicrobial use in food-producing animals` farming systems and environment, animal health, meat production technology and public health. The misuse and overuse of antimicrobials in various sectors, including agriculture and livestock production, have contributed to the emergence and spread of antimicrobial resistance in humans. Antimicrobial use is prevalent in animal husbandry, in particular in intensive farming systems. Antimicrobials and other antimicrobials are often administered to livestock to prevent and treat diseases, as well as promote growth and improve feed efficiency. However, the misuse and excessive use of antimicrobials in animal agriculture have led to the selection and proliferation of resistant bacteria, which can be transmitted to humans through the food (meat) chain via consumption of insufficiently cooked meat or RTE raw fermented meat products, direct contact with animals, or environmental contamination. This can subsequently reduce the efficacy of antimicrobials in human medicine in clinical treatment of patients. Successful tracking of AMR along the meat chain, which encompasses stages `from farm to fork` (farm-abattoir-meat processing-distribution/retail-consumer), should be conducted via application of novel methods, such as WGS and data processing by AI (machine learning algorithms) and based on One Health approach recognizing that the health of humans, animals, and the environment are interconnected. From recently, the special emphasis has been given to the role of environment in development and distribution of AMR. In response to this, four inter-governmental agencies joined their efforts in mitigating AMR from the One Health context, establishing quadripartite initiative, i.e. FAO, WOAH, UNEP and WHO. The EU Commission also encouraged its MSs to develop indicators to measure the performance of their One Health Action Plans on AMR and reduce infections by key resistant microorganisms (e.g. *Campylobacter*, *Salmonella*) in humans and food-producing animals, to improve the adequate and prudent use of antimicrobials in the human and veterinary sectors. In the context of AMR in the meat chain, it emphasizes the need for collaboration and integrated efforts among human health professionals, veterinarians, environmental scientists, policymakers, and other stakeholders to address the complex issue of antimicrobial resistance.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work is supported by the Ministry of Science, Technological Development and Innovations of Republic of Serbia, with reference to the Contract on realization and financing scientific and research work of Scientific Research Organization in 2023., number: 451-03-47/2023-01/200050 from February 3rd 2023.

Author contributions

IN had a role in conceptualization, methodology, data acquisition and analysis, writing original draft, supervision, validation and writing review, editing and providing a critical review; FP participated in data acquisition, writing original draft and validation; KJ contributed in data acquisition and analysis, writing original draft; SVM contributed in data acquisition and analysis, writing original draft, validation and writing review.

List of abbreviations

AI	Artificial Intelligence
AMR	Antimicrobial resistance
AMU	Antimicrobial use
ARG	Antimicrobial resistance genes
AST	Antimicrobial susceptibility testing
CA	Competent Authority
CAB Abstracts	Applied life sciences bibliographic database
CAC	Codex Alimentarius Comission
CCRVDF	Codex Alimentarius Committee on Residues of Veterinary Drugs in Foods
CDC	US Centers for Disease Control and Prevention
CIA	Food and Agriculture Organization list of Critically Important Antibiotics
CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CJWZ	FAO/WHO Centre for Zoonotic Diseases and AMR
CPME	Standing Committee of European Doctors
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Program
EARS-Net	European Antimicrobial Resistance Surveillance Network
EBSCO	Elton B. Stephens Company – information services/scientific databases
EC	European Commission
ECOFFs	Epidemiological cut off values
ECDC	European Centre for Disease Control
EFSA	European Food Safety Authority
EFSA BIOHAZ	European Food Safety Agency Biological Hazards Panel

EMA	European Medicine Agency
EPRUMA	European Platform for the Responsible Use of Medicines in Animals
ESBL	Extended-spectrum β-lactamase-producing *Escherichia coli*
ESVAC	The European Surveillance of Veterinary Antimicrobial Consumption
EU/EEA	European Union/European Economic Area
EUCAST	European Committee on Antimicrobial Resistance Testing
EURL-AR	EU Reference Laboratory for antimicrobial resistance
FAO	UN World Health Organization
FAO AMR	Food and Agriculture Organization Antimicrobial Resistance Action Plan
FAO RENOFARM	FAO initiative to Reduce the Need for Antimicrobials on Farms
FBO	Food business operator
FDA	US Food and Drug Administration
FVE	Federation of Veterinarians of Europe
GAP-AMR	WHO Global Action Plan on AMR
GHP	Good Hygiene Practice
GLASS	WHO Global Antimicrobial Resistance Surveillance System
GMP	Good Manufacturing Practice
GRAS	Generally Recognized as Safe
HACCP	Hazard Analysis and Critical Control Points
HIH	FAO \`Hand-in-Hand\` Initiative to accelerate agrifood systems transformations by eradicating poverty (SDG1), ending hunger and malnutrition (SDG2), and reducing inequalities (SDG10)
HDI	UN Human Development Index
IACG	UN Interagency coordination group
IZD	Inhibition zone diameters
LAB	Lactic Acid Bacteria
MARAN	Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands
MIC	Minimum inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSs	EU Member States
NARMS	US National Antimicrobial Resistance Monitoring System
NCP	National Control Programme
NETHMAP	Consumption of Antimicrobial Agents and Antimicrobial Resistance among Medically Important Bacteria in the Netherlands
NORM-Vet	Usage of Antimicrobial Agents and Occurrence of Antimicrobial Resistance in Norway
OH	One Health approach
OHHLEP	FAO/WHO/UNEP/WOAH One Health High-Level Expert Panel
PCU	Population Correction Unit
SRS	Simple random sampling
QPS	Qualified Presumption of Safety
RESAPATH	French surveillance network for antimicrobial resistance in pathogenic bacteria of animal origin
RONAFA	EMA and EFSA joint scientific opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the EU and the resulting impacts on food safety
RTE	Ready-To-Eat
SARS-CoV2	Severe Acute Respiratory Syndrome Coronavirus 2
Scopus	Elsevier‘s abstract and citation database
SDGs	UN Sustainable Development Goals
SDG1	Sustainable Development Goal 1: Eradicating poverty
SDG2	Sustainable Development Goal 2: Ending hunger and malnutrition
SDG10	Sustainable Development Goal 10: Reducing inequalities
SVARM	Swedish Veterinary Antimicrobial Resistance Monitoring
SWEDRES	Swedish Antibiotic Utilisation and Resistance in Human Medicine
UNEP	UN Environment Programme
USDA	United States Department of Agriculture
VCIA	Veterinary Critically Important Antimicrobial Agents
VHIA	Veterinary Highly Important Antimicrobial Agents
VIA	Veterinary Important Antimicrobial Agents
VMPs	Veterinary medicinal products
Web of Science	Platform for access to multiple databases that provide reference and citation data from academic journals, conference proceedings, academic disciplines
WGS	Whole Genome Sequencing
WHO	UN World Health Organization

WOAH (OIE)	World Organisation for Animal Health, founded as `Office International des Épizooties` (OIE) in 1924.

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